REMARKS

Reconsideration of the above-identified application in view of the remarks following is respectfully requested.

Claims 1-11 are in this case. Claims 4-11 were withdrawn under a restriction requirement as drawn to a non-elected invention. Claims 1-3 have been rejected. Claims 1-3 have now been amended.

35 U.S.C. § 102(b) Rejections

The Examiner has rejected claims 1-3 under 35 U.S.C. § 102(b) as being anticipated by Mottez et al [J. Exp. Med (1995) 181: 493-502]. The Examiner's rejections are respectfully traversed.

The Examiner points out that Mottez teaches single chain constructs comprising an MHC class I heavy chain joined to β2-microglobulin with a covalently bound antigenic peptide and that linker or spacer sequences separate the segments. The Examiner states that the prior art teaching anticipates the claimed invention.

Applicant agrees with the Examiner that Mottez describes the construction of a single polynucleotide encoding a mouse MHC molecule covalently bound to an antigenic peptide. Mottez et al constructed a DNA construct in which the oligonucleotide sequence encoding the antigenic peptide is ligated between signal sequence and the mature sequence of the murine MHC Kd molecule, which are further ligated to the sequence encoding the murine β2 microglobulin. Following the expression of such a DNA construct in eukaryotic cells (*e.g.*, mouse L cells and CHO cells) Mottez et al., detected the antigenic peptide on the cell surface of the transfected cells and mistakenly assumed that the recombinant antigenic peptide is presented on the recombinant MHC I complex. In fact, since eukaryotic cells include endogenous MHC I complexes and a developed proteosome machinery, following the expression of such a DNA construct which encodes the MHC I complex bound to the antigenic peptide, the recombinant MHC I complex is degraded by the endogenous proteosome machinery and the degraded antigenic peptide, which exhibits the inherent properties of a class I MHC peptide, is further presented by the endogenous MHC I complex on the transfected cells. Thus, expression of the construct used by the prior art in eukaryotic cells did not result in an isolated chimeric and functional MHC I complex

and the teachings of this prior art would not lead an ordinary skilled artisan to generate such isolated polypeptide.

In sharp contrast to the reference cited by the Examiner, the present invention relates to an isolated chimeric polypeptide comprising an antigenic peptide being capable of binding a human MHC class I, a functional human β-2 microglobulin and a functional human MHC class I heavy chain. In the present study the isolated chimeric polypeptide is produced from a DNA construct encoding the human β-2 microglobulin, the human MHC class I heavy chain and the antigenic peptide in a 1:1:1 ratio. In order to form the isolated chimeric polypeptide of the present invention such a DNA construct is expressed in bacteria which lacks the proteosome machinery and thus enables the formation of a functional, recombinant single chain MHC I complex, which is capable of the biological activity [e.g., interact with T cell receptor (TCR) and activate specific cytotoxic T-cells (CTLs)]. In this unique and unexpected expression system, following the expression of the recombinant MHC I complex in the host cells, the synthesized protein is concentrated as insoluble inclusion bodies which are further recovered and refolded to produce functional and stable MHC I complexes (See enclosed declaration and manuscript).

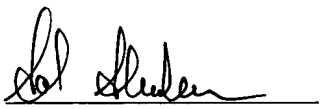
It will be appreciated that although the mouse and human MHC I molecules are homologous, there are some significant differences between these sequences, especially in the antigenic peptide binding region (Paul W, Fundamental Immunology, Lippincott –Raven 1999, page 263-286) which determines which peptide binds to the peptide-binding groove and thus controls the specificity of MHC presentation. In addition, the human and murine β-2 microglobulin polypeptides are different in their ability to stabilize the MHC I complex [Paul W, 1999 (Supra)].

Thus, due to the fact that the prior art teaches an expression system which cannot be utilized to produce the isolated and functional polypeptide of the present invention, and further due to the fact that there are structural and functional differences between the human and murine MHC complex, Applicant strongly believes that *in vitro* generation and isolation of a single polypeptide that represents a functional human MHC I complex is neither anticipated not rendered obvious by prior art attempts to generate a mouse MHC I complex.

Thus, in contrast to Examiner's statement, the isolated chimeric polypeptide of the present invention which includes a functional human MHC I complex, a functional human β-2 microglobulin and an antigenic peptide is novel.

In view of the above remarks it is respectfully submitted that claims 1-3 are now in condition for allowance. Prompt Notice of Allowance is respectfully and earnestly solicited.

Respectfully submitted,



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Encl.
Extension fee: one month
Manuscript - Oved K., et al.
Declaration by Yoram Reiter